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09/485,298	02/08/00	YAMAMOTO	J 1423-411F

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EXAMINER	
CHAKRABARTI, A	
ART UNIT	PAPER NUMBER
1655	8
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

<b>Office Action Summary</b>	Application No. 09/485,298	Applicant(s) Yamamoto et al.
	Examiner Arun Chakrabarti	Group Art Unit 1655

*Responsive to communication(s) filed on Sep 28, 2000*

*This action is FINAL.*

*Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.*

*A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).*

#### Disposition of Claims

*Claim(s) 17-37* is/are pending in the application.

*Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.*

*Claim(s) \_\_\_\_\_ is/are allowed.*

*Claim(s) 17-37* is/are rejected.

*Claim(s) \_\_\_\_\_ is/are objected to.*

*Claims \_\_\_\_\_ are subject to restriction or election requirement.*

#### Application Papers

*See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.*

*The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.*

*The proposed drawing correction, filed on \_\_\_\_\_ is  approved  disapproved.*

*The specification is objected to by the Examiner.*

*The oath or declaration is objected to by the Examiner.*

#### Priority under 35 U.S.C. § 119

*Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).*

*All  Some\*  None of the CERTIFIED copies of the priority documents have been received.*

*received in Application No. (Series Code/Serial Number) \_\_\_\_\_.*

*received in this national stage application from the International Bureau (PCT Rule 17.2(a)).*

\*Certified copies not received: \_\_\_\_\_

*Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).*

#### Attachment(s)

*Notice of References Cited, PTO-892*

*Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_*

*Interview Summary, PTO-413*

*Notice of Draftsperson's Patent Drawing Review, PTO-948*

*Notice of Informal Patent Application, PTO-152*

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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**DETAILED ACTION**

***Priority***

1. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 9-231885, filed on August 14, 1997 in Japan.

***Specification***

2. Claims 1-16 have been canceled without prejudice towards further prosecution. New claims 17-37 have been added.

***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

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invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 17-25 and 27-29 are rejected under 35 U.S.C 103 (a) over Dower et al. (U.S. Patent 5,639,603) (June 17, 1997) in view of Koster et al. (U.S.Patent 6,043,031) (March 28, 2000).

Dower et al teach a method for amplifying a DNA by polymerase chain reaction by the use of a DNA fragment comprising a nucleotide analog as a template (Column 27, lines 3-30).

Dower et al teach a method for amplifying a DNA characterized in that the DNA fragment is a cDNA prepared by reverse transcription reaction using an RNA as a template (Column 35, lines 40-64).

Dower et al do not teach the method for amplifying a DNA in the presence of two or more kinds of nucleotide analogs.

Koster et al teach the method for amplifying a DNA in the presence of two or more kinds of nucleotide analogs (7-Deaza-dGTP) to be incorporated in a DNA strand in place of dGTP and at least one nucleotide analog is incorporated in the amplifying step in place of dATP (Example 8, Column 30, line 64 to column 33, line 27 and Table 1). In addition, Koster et al teach a template containing nucleotide analog formed during PCR (Column 33, lines 12-16).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the modified nucleotide analogues model of Koster et al with the methods of amplifying nucleic acids using modified nucleotide template of

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Dower et al ., since Koster et al state, "The process of the invention provide for increased accuracy and reliability of nucleic acid detection. In addition, the process allows for rigorous controls to prevent false negative or positive results. The processes of the invention avoid electrophoretic steps; labeling and subsequent detection of a label. In fact it is estimated that the entire procedure, including nucleic acid isolation, amplification, and mass spec analysis requires only about 2-3 hours time. Therefore, the instant disclosed processes of the invention are faster and less expensive to perform than existing DNA detection systems. In addition, because the instant disclosed processes allow the nucleic acid fragments to be identified and detected at the same time by their specific molecular weights (an unambiguous physical standard), the disclosed processes are also much more accurate and reliable than currently available procedures (Column 5, lines 26-42)". An ordinary artisan would have been motivated by these express statements of Koster et al to combine the modified nucleotide analogues model of Koster et al with the methods of amplifying nucleic acids using modified nucleotide template of Dower et al., in order to achieve the express advantages of modified nucleotide analogues, as noted by Koster et al , which provides for increased accuracy and reliability of nucleic acid detection and in addition allows for rigorous controls to prevent false negative or positive results which avoids electrophoretic steps; labeling and subsequent detection of a label and which are faster and less expensive to perform than existing DNA detection systems and in addition which allows the nucleic acid fragments to be identified and detected at the same time by their specific molecular

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weights (an unambiguous physical standard) thereby rendering the process also much more accurate and reliable than currently available procedures.

5. Claims 17-30 are rejected under 35 U.S.C 103 (a) over Dower et al. (U.S. Patent 5,639,603) (June 17, 1997) in view of Koster et al. (U.S. Patent 6,043,031) (March 28, 2000) further in view of Dodge et al. (U.S. Patent 5,912,117) (June 15, 1999).

Dower et al in view of Koster et al teach the method of claims 17-25 and 27-29 as described above.

Dower et al in view of Koster et al do not teach the compounds for lowering the *Tm* value of a double-stranded nucleic acid.

Dodge et al teach the compounds (glycerol and DMSO) for lowering the *Tm* value of a double-stranded nucleic acid.(Column 8, line 49 to column 9, line 4).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the compounds for lowering Tm of duplex DNA of Dodge et al with the fast and accurate methods of amplifying nucleic acids using modified nucleotide template and nucleotides of Dower et al in view of Koster et al., since Dodge et al state, "To assure PCR efficiency, glycerol and other related solvents such as dimethyl sulfoxide, can be used to increase the sensitivity of the PCR at the amplification level and to overcome problems pertaining to the sequencing of regions of DNA having strong secondary structure. These problems may include : (1) low efficiency of the PCR, due to a high frequency of templates that are not fully extended by the polymerizing agent or (2) incomplete denaturation

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of the duplex DNA at high temperatures, due to high GC content. The use of such solvents increases the sensitivity of the assay at the level of amplification to approximately several femtograms of DNA (which is believed to correspond to a single spirochete cell). This level of sensitivity eliminates the need to detect amplified target DNA using a probe, and thereby dispenses with the requirements for radioactive probes, gel electrophoresis, Southern blotting, filter hybridization, washing and autoradiography (Column 8, line 49 to column 9, line 2)". An ordinary artisan would have been motivated by these express statements of Dodge et al to substitute and combine the compounds for lowering Tm of duplex DNA of Dodge et al with the fast and accurate methods of amplifying nucleic acids using modified nucleotide template and nucleotides of Dower et al in view of Koster et al., in order to achieve the express advantages of solvents, as noted by Dodge et al , which provides assurance of PCR efficiency and increases the sensitivity of the PCR at the amplification level to overcome problems pertaining to the sequencing of regions of DNA having strong secondary structure including : (1) low efficiency of the PCR, due to a high frequency of templates that are not fully extended by the polymerizing agent or (2) incomplete denaturation of the duplex DNA at high temperatures, due to high GC content and in addition, increases the sensitivity of the assay at the level of amplification to approximately several femtograms of DNA (which is believed to correspond to a single spirochete cell) which eliminates the need to detect amplified target DNA using a probe, and thereby dispenses with the requirements for radioactive probes, gel electrophoresis, Southern blotting, filter hybridization, washing and autoradiography.

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6. Claims 17-37 are rejected under 35 U.S.C 103 (a) over Dower et al. (U.S. Patent 5,639,603) (June 17, 1997) in view of Koster et al. (U.S. Patent 6,043,031) (March 28, 2000) further in view of Dodge et al. (U.S. Patent 5,912,117) (June 15, 1999) further in view of Stratagene Catalog (1988, Page 39).

Dower et al. in view of Koster et al. further in view of Dodge et al. expressly teach the method claims of 17-30 including all the modified nucleotide templates, analogues and compounds for lowering the *Tm* value of a double-stranded nucleic acid as described above in detail.

Dower et al. in view of Koster et al. further in view of Dodge et al do not teach the motivation to combine all the reagents for amplifying a nucleic acid in the form of a kit.

Stratagene catalog teaches a motivation to combine reagents into kit format (page 39).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine a suitable container and all the modified nucleotide templates, analogues and compounds for lowering the *Tm* value of a double-stranded nucleic acid as taught by Dower et al. in view of Koster et al. further in view of Dodge et al. into a kit format as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. Thus one need not purchase gram quantities of 10 different reagents, each of which is needed in only microgram amounts, when beginning a series of experiments. When one

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considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually far more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantities you will actually need, premixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2) The other service provided in a kit is "quality control". (page 39, column 1).

### ***Conclusion***

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

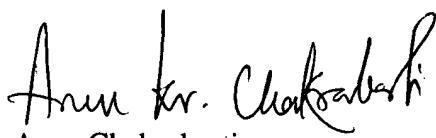
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.



Arun Chakrabarti,

Patent Examiner,

October 19, 2000



JEFFREY FREDMAN  
PRIMARY EXAMINER